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UNCATALYZED ADDITION OF ALCOHOLS AND AMINES TO THE C=N BOND OF THE MONOIMINE FROM BENZIL AND 2-AMINOPYRIDINE

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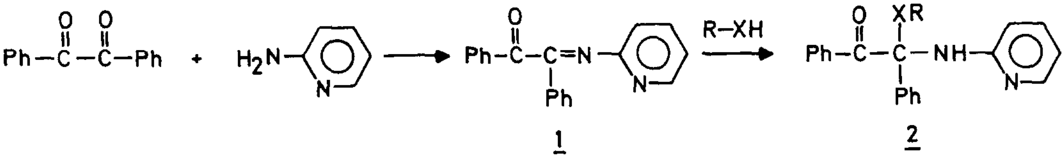
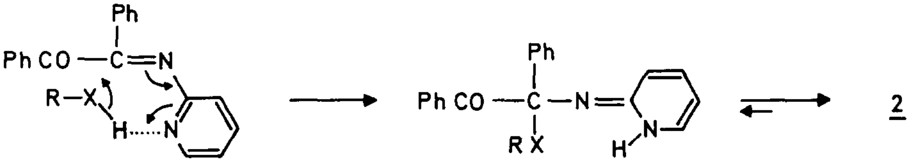
Summary: *The monoimine easily formed by direct condensation between benzil and 2-aminopyridine adds alcohols and amines to the imine bond without catalysis. A concerted mechanism is proposed.*

Although base-catalyzed additions of alcohols to the imine C=N bond have been studied in some detail,[1] very few examples have been reported of the related uncatalyzed addition.[2] We have found that the monoimine obtained by direct condensation between benzil and 2-aminopyridine,[3] 1, undergoes uncatalyzed addition of alcohols and amines. Quantitative yields of addition products, 2, were obtained (Scheme I; table). Electronic withdrawing by the pyridine ring is not the main reason for the addition since, in the same reaction conditions, the monoimine obtained from benzil and p-nitroaniline gave no reaction.



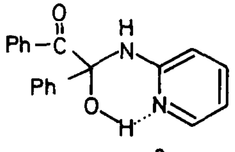
Scheme I

We propose the reaction course shown in Scheme II which involves a three electron pairs concerted displacement, favoured by the molecular association of the alcohol or amine to the pyridine nitrogen atom.



Scheme II

The easy reaction between benzil and 2-aminopyridine is noteworthy, as compared with its 3- and 4-homologues which failed to react even in stronger conditions. It is considered that stabilization of the intermediate carbinolamine,



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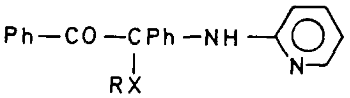
3, through intramolecular hydrogen bonding would favour the addition process;[4] this, of course, is not possible for the 3- and 4-aminopyridines.

Spectral data of addition compound 2d (see table) show a similar association.[5]

Table

Addition Compounds of Alcohols and Amines to the Monoimine of Benzil and 2-Aminopyridine



$$\underset{\displaystyle RX}{\mathrm{Ph{-}CO{-}CPh{-}NH{-}C_5H_4N}}$$

2

Comp.	X	R	m.p.	i.r.[a]	^{1}H n.m.r.[b]	Analysis	
						Calc.	Found
2a	0	CH_3	130-132°	$\nu_{C=0}$ 1720 ν_{N-H} 3370	3.56 (s, 3H) 5.8-7.6 (m, 14H) 7.8 (d, 1H) J=4 Hz	C, 75.47 H, 5.66 N, 8.81	75.19 5.81 8.95
2b	0	CH_3CH_2	68-70°	$\nu_{C=0}$ 1725 ν_{N-H} 3370	1.0 (t, 3H) J=7.7 Hz 4.2 (q, 2H) J=7.7 Hz 5.9-7.7 (m, 14H) 8.0 (d, 1H) J=4 Hz	C, 75.90 H, 6.02 N, 8.43	75.76 6.17 8.51
2c[c]	0	$C_6H_5CH_2$	110-111°	$\nu_{C=0}$ 1750 ν_{N-H} 3439	5.13 (s, 2H) 5.9-7.7 (m, 19H) 8.0 (d, 1H) J=4 Hz	C, 79.39 H, 5.34 N, 7.12	79.61 5.24 7.15
2d[d]	NH	$C_6H_5CH_2$	180°	$\nu_{C=0}$ 1670 ν_{N-H} 3260 (broad) 3420 (sharp)	4.4 (d, 2H) J=4 Hz 6.4-7.7 (m, 19H) 7.9 (d, 1H) J=3 Hz 8.4 (t, 1H) J=4 Hz	C, 79.39 H, 5.85 N, 10.89	79.19 5.83 10.70

a) KBr crystals. *b)*60 MHz; in $CDCl_3$ solution. *c)* Yield: 85%. *d)* ^{1}H n.m.r. at 90 MHz in DMSO-d^6 solution; see ref. 5.

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References and Notes

1. Y. Ogata and A. Kawasaki, J. Org. Chem., 39, 1058, (1974).
2. S. Miyano and N. Abe, Tetrahedron Letters, 1909, (1970); W. R. Mc Kay, and G. R. Proctor, J. Chem. Soc. Perkin Trans I, 2443, (1981).
3. In boiling xylene. Reaction time: 7.5 hrs. Catalyst: $ZnCl_2$·1-phenylethylamine complex. Equimolar amounts of benzil and 2-aminopyridine (42.6 mmol of each in 70 ml. of solvent). Yield: 85% of pure product. Yellow crystals from n-hexane/AcOEt 1:2, m.p. 115-116°. i.r. (KBr): ν(C=0), 1758 cm^{-1}, ν(C=N), 1649 cm^{-1}. ^{13}C n.m.r.: δ(C=0), 180.02, δ(C=N), 155.54. Analysis: Calc. for $C_{19}H_{14}N_2O$: C, 79.72; H, 4.80; N, 9.79. Found: C, 79.97; H, 4.76; N, 9.58.
4. For the mechanism of Schiff bases formation see, for example, S. Patai: "The Chemistry of the C=N Group", Interscience, 1970.

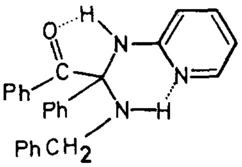

Fig.

5. ^{1}H n.m.r. data for 2d show a significant coupling through nitrogen. Signals at 7.9 and 8.4 are not interchanged with D_2O. This is an indication of the presence of a strongly associated structure as shown in Figure.

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